

=> fil reg

FILE 'REGISTRY' ENTERED AT 09:03:00 ON 14 MAR 2005

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STRUCTURE FILE UPDATES: 13 MAR 2005 HIGHEST RN 845467-46-1

DICTIONARY FILE UPDATES: 13 MAR 2005 HIGHEST RN 845467-46-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d l19 ide can

L19 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN

RN 294849-86-8 REGISTRY

CN Urea, N-[5-(1;1-dimethylethyl)-2-methylphenyl]-N'-[4-[6-[(3-methoxypropyl)methylamino]-3-pyridinyl]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C32 H38 N4 O2

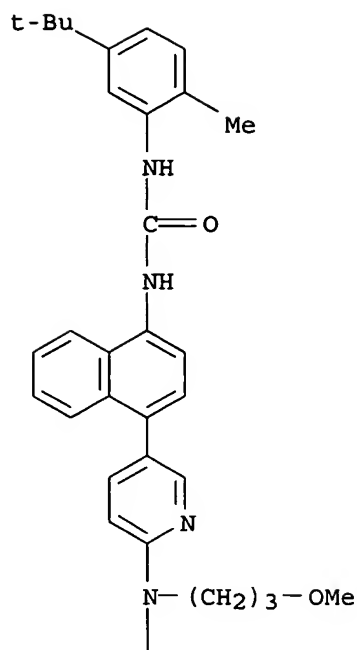
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

DT.CA CAPLUS document type: Patent

RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:197476

REFERENCE 2: 133:252426

=> d his

(FILE 'HOME' ENTERED AT 08:52:21 ON 14 MAR 2005)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 08:52:37 ON 14 MAR 2005

L1 3 S (US20040019038 OR US6660732 OR US20020055507 OR US6656933 OR
E CIRILLO P/AU
L2 48 S E3,E6-E8
E BREITFELDER S/AU
L3 19 S E5,E6
E PATEL U/AU
L4 58 S E3,E12,E37,E41,E42
E PROUDFOOT J/AU
L5 261 S E3,E5,E7-E9
E SWINAMER A/AU

L6 9 S E4-E6
E TAKAHASHI H/AU
L7 1739 S E3-E8,E95-E97
E GILMORE T/ AU
L8 44 S E3,E4,E11,E12,E21
E SHARMA R/AU
L9 3007 S E3-E26,E94-E97
E BOHRING/PA,CS
L10 10 S E3-E12
E BEOHRING/PA,CS
E BOEHRING/PA,CS
L11 8534 S BOEHRING?/PA,CS
L12 3 S L1 AND L2-L11
SEL RN

FILE 'REGISTRY' ENTERED AT 08:59:15 ON 14 MAR 2005

L13 347 S E1-E347
L14 151 S L13 AND 46.150.18/RID AND C6-C6/ES AND NC5/ES
L15 8 S L14 AND 4/NR
L16 1 S L15 AND C32H38N4O2
L17 0 S 294849-86-8/CRN
E C32H38N4O2/MF
L18 1 S E3 AND 46.150.18/RID AND C6-C6/ES AND NC5/ES
L19 1 S L16,L18

FILE 'HCAOLD' ENTERED AT 09:02:13 ON 14 MAR 2005

L20 0 S L19

FILE 'USPATFULL' ENTERED AT 09:02:14 ON 14 MAR 2005

L21 6 S L19

FILE 'HCAPLUS' ENTERED AT 09:02:35 ON 14 MAR 2005

L22 2 S L19
L23 1 S L22 AND L1-L12
L24 2 S L22,L23

FILE 'REGISTRY' ENTERED AT 09:03:00 ON 14 MAR 2005

=> fil uspatful

FILE 'USPATFULL' ENTERED AT 09:03:07 ON 14 MAR 2005

CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 10 Mar 2005 (20050310/PD)

FILE LAST UPDATED: 10 Mar 2005 (20050310/ED)

HIGHEST GRANTED PATENT NUMBER: US6865747

HIGHEST APPLICATION PUBLICATION NUMBER: US2005055750

CA INDEXING IS CURRENT THROUGH 10 Mar 2005 (20050310/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 10 Mar 2005 (20050310/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2005

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2005

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>>> USPAT2 is now available.  USPATFULL contains full text of the  <<<
>>> original, i.e., the earliest published granted patents or  <<<
>>> applications.  USPAT2 contains full text of the latest US  <<<
>>> publications, starting in 2001, for the inventions covered in  <<<
>>> USPATFULL.  A USPATFULL record contains not only the original  <<<
>>> published document but also a list of any subsequent  <<<
>>> publications.  The publication number, patent kind code, and  <<<
>>> publication date for all the US publications for an invention  <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL  <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc.  <<<
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>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<
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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l21 bib abs hitstr tot

L21 ANSWER 1 OF 6 USPATFULL on STN

AN 2004:31819 USPATFULL

TI Aryl ureas with raf kinase and angiogenesis inhibiting activity

IN Dumas, Jacques, Bethany, CT, UNITED STATES

Scott, William J., Guilford, CT, UNITED STATES

Elting, James, Madison, CT, UNITED STATES

Hatoum-Makdad, Holia, Hamden, CT, UNITED STATES

PA BAYER CORPORATION, Pittsburgh, PA (U.S. corporation)

PI US 2004023961 A1 20040205

AI US 2003-361844 A1 20030211 (10)

PRAI US 2002-354948P 20020211 (60)

DT Utility

FS APPLICATION

LREP MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE
1400, ARLINGTON, VA, 22201

CLMN Number of Claims: 46

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 4402

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to methods of using aryl ureas to treat diseases mediated by raf kinase and diseases mediated by the VEGF induced signal transduction pathway characterized by abnormal angiogenesis or hyperpermeability processes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

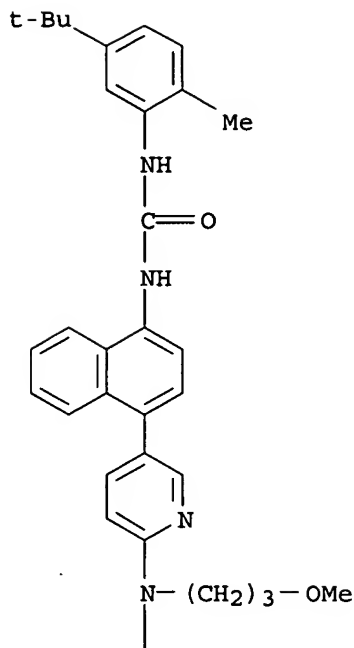
IT 294849-86-8P

(preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

RN 294849-86-8 USPATFULL

CN Urea, N-[5-(1,1-dimethylethyl)-2-methylphenyl]-N'-[4-[6-[(3-methoxypropyl)methylamino]-3-pyridinyl]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L21 ANSWER 2 OF 6 USPATFULL on STN
 AN 2004:25196 USPATFULL
 TI Compounds useful as anti-inflammatory agents
 IN Cirillo, Pier F., Woodbury, CT, UNITED STATES
 Breitfelder, Steffen, Assmannshardt, GERMANY, FEDERAL REPUBLIC OF
 Patel, Usha R., Brookfield, CT, UNITED STATES
 Proudfoot, John Robert, Newtown, CT, UNITED STATES
 Swinamer, Alan D., Bethel, CT, UNITED STATES
 Takahashi, Hidenori, LaGrangeville, NY, UNITED STATES
 Gilmore, Thomas A., Cambridge, MA, UNITED STATES
 Sharma, Rajiv, Foster City, CA, UNITED STATES
 PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, UNITED
 STATES, 06877-0368 (U.S. corporation)
 PI US 2004019038 A1 20040129
 AI US 2003-624289 A1 20030721 (10)
 RLI Division of Ser. No. US 2001-962709, filed on 25 Sep 2001, GRANTED, Pat.
 No. US 6660732 Division of Ser. No. US 2000-505582, filed on 16 Feb
 2000, GRANTED, Pat. No. US 6358945
 PRAI US 1999-124148P 19990312 (60)
 US 1999-165867P 19991116 (60)
 DT Utility
 FS APPLICATION
 LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368,
 RIDGEFIELD, CT, 06877
 CLMN Number of Claims: 22
 ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 6759

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are novel aromatic compounds which are useful for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are pharmaceutical compositions containing and processes of making such compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

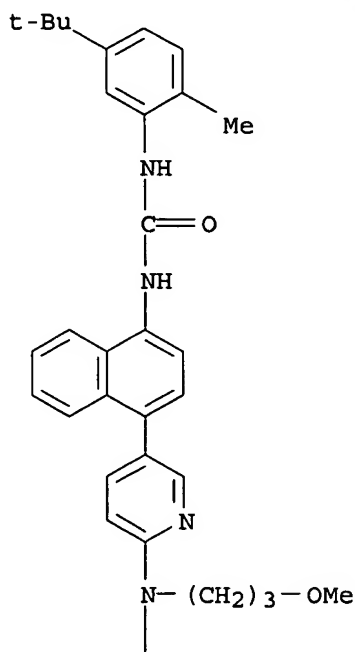
IT 294849-86-8P

(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)

RN 294849-86-8 USPATFULL

CN Urea, N-[5-(1,1-dimethylethyl)-2-methylphenyl]-N'-[4-[6-[(3-methoxypropyl)methylamino]-3-pyridinyl]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L21 ANSWER 3 OF 6 USPATFULL on STN

AN 2003:319328 USPATFULL

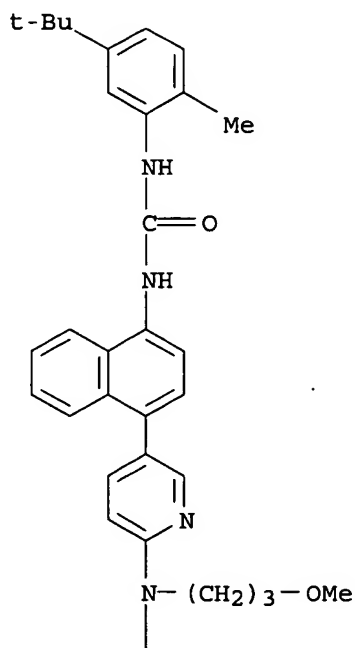
TI Intermediate arylamine compounds

IN Cirillo, Pier F., Woodbury, CT, UNITED STATES
 Breitfelder, Steffen, Ridgefield, CT, UNITED STATES
 Patel, Usha R., Brookfield, CT, UNITED STATES
 Proudfoot, John R., Newtown, CT, UNITED STATES
 Swinamer, Alan D., Danbury, CT, UNITED STATES

PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT (U.S. corporation)
PI US 2003225077 A1 20031204
AI US 2003-424613 A1 20030428 (10)
RLI Continuation of Ser. No. US 2001-962057, filed on 25 Sep 2001, PENDING
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368, RIDGEFIELD, CT, 06877
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5832
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic compounds which are useful for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are and pharmaceutical compositions containing, intermediate compounds and processes of making such compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 294849-86-8P
(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)
RN 294849-86-8 USPATFULL
CN Urea, N-[5-(1,1-dimethylethyl)-2-methylphenyl]-N'-[4-[6-[(3-methoxypropyl)methylamino]-3-pyridinyl]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



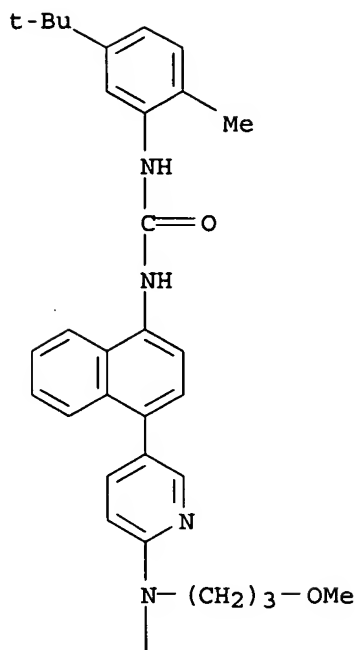
PAGE 2-A

Me

L21 ANSWER 4 OF 6 USPATFULL on STN
AN 2002:157650 USPATFULL
TI Compounds useful as anti-inflammatory agents
IN Betageri, Rajashehar, Bethel, CT, UNITED STATES
Breitfelder, Steffen, Danbury, CT, UNITED STATES
Cirillo, Pier F., Woodbury, CT, UNITED STATES
Gilmore, Thomas A., Middlebury, CT, UNITED STATES
Hickey, Eugene R., Danbury, CT, UNITED STATES
Kirrane, Thomas M., JR., Danbury, CT, UNITED STATES
Moriak, Monica H., Danbury, CT, UNITED STATES
Moss, Neil, Ridgefield, CT, UNITED STATES
Patel, Usha R., Brookfield, CT, UNITED STATES
Proudfoot, John R., Newtown, CT, UNITED STATES
Regan, John R., Larchmont, NY, UNITED STATES
Sharma, Rajiv, Ridgefield, CT, UNITED STATES
Sun, Sanxing, Danbury, CT, UNITED STATES
Swinamer, Alan D., Danbury, CT, UNITED STATES
Takahashi, Hidenori, LaGrangeville, NY, UNITED STATES
PI US 2002082256 A1 20020627
US 6656933 B2 20031202
AI US 2001-962057 A1 20010925 (9)
RLI Division of Ser. No. US 2000-505582, filed on 16 Feb 2000, PENDING
PRAI US 1999-124148P 19990312 (60)
US 1999-165867P 19991116 (60)
DT Utility
FS APPLICATION
LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368,
RIDGEFIELD, CT, 06877
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6137
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic compounds which are useful for treating
diseases or pathological conditions involving inflammation such as
chronic inflammatory diseases. Also disclosed are pharmaceutical
compositions containing and processes of making such compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 294849-86-8P
(preparation of aromatic heterocyclic urea antiinflammatory agents by
conversion of arylamines to isocyanates followed by addition of
heterocyclic amines)
RN 294849-86-8 USPATFULL
CN Urea, N-[5-(1,1-dimethylethyl)-2-methylphenyl]-N'-[4-[6-[(3-
methoxypropyl)methylamino]-3-pyridinyl]-1-naphthalenyl]- (9CI) (CA
INDEX NAME)

PAGE 1-A



PAGE 2-A



L21 ANSWER 5 OF 6 USPATFULL on STN
 AN 2002:106298 USPATFULL
 TI Compounds useful as anti-inflammatory agents
 IN Betageri, Rajashehar, Bethel, CT, UNITED STATES
 Breitfelder, Steffen, Danbury, CT, UNITED STATES
 Cirillo, Pier F., Woodbury, CT, UNITED STATES
 Gilmore, Thomas A., Middlebury, CT, UNITED STATES
 Hickey, Eugene R., Danbury, CT, UNITED STATES
 Kirrane, Thomas M., Danbury, CT, UNITED STATES
 Moriak, Monica H., Danbury, CT, UNITED STATES
 Moss, Neil, Ridgefield, CT, UNITED STATES
 Patel, Usha R., Brookfield, CT, UNITED STATES
 Proudfoot, John R., Newtown, CT, UNITED STATES
 Regan, John R., Larchmont, NY, UNITED STATES
 Sharma, Rajiv, Ridgefield, CT, UNITED STATES
 Sun, Sanxing, Danbury, CT, UNITED STATES
 Swinamer, Alan D., Danbury, CT, UNITED STATES
 Takahashi, Hidenori, LaGrangeville, NY, UNITED STATES
 PI US 2002055507 A1 20020509
 US 6660732 B2 20031209
 AI US 2001-962709 A1 20010925 (9)
 RLI Division of Ser. No. US 2000-505582, filed on 16 Feb 2000, PENDING
 PRAI US 1999-124148P 19990312 (60)
 US 1999-165867P 19991116 (60)
 DT Utility
 FS APPLICATION

LREP BOEHRINGER INGELHEIM CORPORATION, 900 RIDGEBURY ROAD, P O BOX 368,
 RIDGEFIELD, CT, 06877
 CLMN Number of Claims: 22
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 6968
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB Disclosed are novel aromatic compounds which are useful for treating
 diseases or pathological conditions involving inflammation such as
 chronic inflammatory diseases. Also disclosed are pharmaceutical
 compositions containing and processes of making such compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

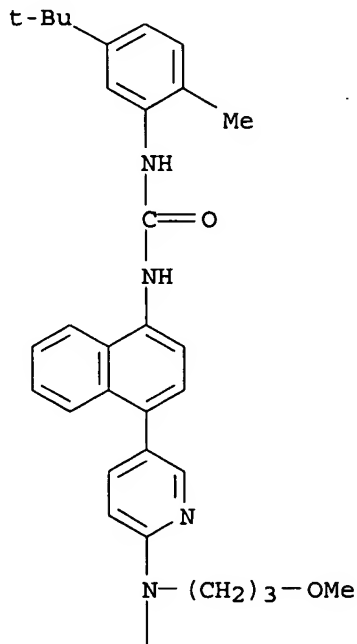
IT 294849-86-8P

(preparation of aromatic heterocyclic urea antiinflammatory agents by
 conversion of arylamines to isocyanates followed by addition of
 heterocyclic amines)

RN 294849-86-8 USPATFULL

CN Urea, N-[5-(1,1-dimethylethyl)-2-methylphenyl]-N'-[4-[6-[(3-
 methoxypropyl)methylamino]-3-pyridinyl]-1-naphthalenyl]- (9CI) (CA
 INDEX NAME)

PAGE 1-A



PAGE 2-A

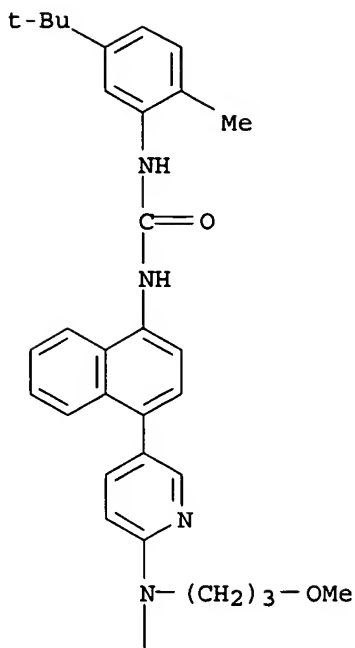
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L21 ANSWER 6 OF 6 USPATFULL on STN
 AN 2002:57780 USPATFULL
 TI Compounds useful as anti-inflammatory agents
 IN Breitfelder, Steffen, Danbury, CT, United States

Cirillo, Pier F., Woodbury, CT, United States
Gilmore, Thomas A., Middlebury, CT, United States
Hickey, Eugene R., Danbury, CT, United States
Proudfoot, John R., Newtown, CT, United States
Regan, John R., Larchmont, NY, United States
Swinamer, Alan D., Danbury, CT, United States
Takahashi, Hidenori, LaGrangeville, NY, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 6358945 B1 20020319
AI US 2000-505582 20000216 (9)
PRAI US 1999-124148P 19990312 (60)
US 1999-165867P 19991116 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Raymond, Richard L.
LREP Raymond, Robert P., Bottino, Anthony P., Stempel, Alan R.
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 6875
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are novel aromatic compounds which are useful for treating diseases or pathological conditions involving inflammation such as chronic inflammatory diseases. Also disclosed are pharmaceutical compositions containing and processes of making such compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 294849-86-8P
(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)
RN 294849-86-8 USPATFULL
CN Urea, N-[5-(1,1-dimethylethyl)-2-methylphenyl]-N'-[4-[6-[(3-methoxypropyl)methylamino]-3-pyridinyl]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



=> fil hcaplus
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FILE COVERS 1907 - 14 Mar 2005 VOL 142 ISS 12
FILE LAST UPDATED: 13 Mar 2005 (20050313/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot 124

L24 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2003:656575 HCAPLUS
 DN 139:197476
 ED Entered STN: 22 Aug 2003
 TI Preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis
 inhibiting activity
 IN Dumas, Jacques; Scott, William J.; Elting, James; Hatoum-Makdad, Holia
 PA Bayer Corporation, USA
 SO PCT Int. Appl., 142 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-415
 ICS A61K031-5355; A61K031-4439; A61K031-4178; A61P035-00; A61P017-06;
 A61P019-02; A61P027-02; A61P031-06; A61P031-18; A61P031-04
 CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 63

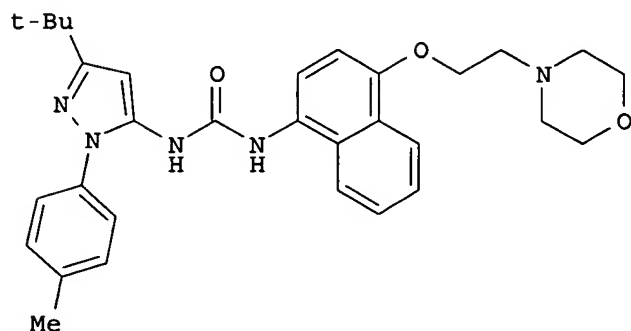
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	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003068223	A1	20030821	WO 2003-US4102	20030211
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	US 2004023961	A1	20040205	US 2003-361844	20030211
PRAI	US 2002-354948P	P	20020211		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003068223	ICM	A61K031-415
	ICS	A61K031-5355; A61K031-4439; A61K031-4178; A61P035-00; A61P017-06; A61P019-02; A61P027-02; A61P031-06; A61P031-18; A61P031-04

GI



I

AB 283 Of the title ureas useful for treating diseases mediated by raf kinase and diseases mediated by the VEGF induced signal transduction pathway

characterized by abnormal angiogenesis or hyperpermeability processes, were claimed. Synthesis of 6 ureas such as I was described. Thus, reacting 3-(tert-butyl)-1-(4-methylphenyl)pyrazole-5-ylamine with 4-(2-morpholin-4-ylethoxy)naphthylamine (prepns. given) and CDI in CH₂Cl₂ afforded 80% I which showed IC₅₀ of < 1 μ M in in vitro raf kinase and in in vitro Flk-1 ELISA assay.

- ST aryl heterocyclyl urea prepn raf kinase angiogenesis inhibitor; pyrazolyl aryl urea prepn tyrosine kinase Flk1 KDR; antitumor aryl heterocyclyl urea prepn; VEGF induced signal transduction pathway aryl heterocyclyl urea prepn
- IT Infection
(Chagas' disease, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Intercalation compounds
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA intercalators; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity for treating hyper-proliferative disorder in combination with addnl. cytotoxic agent or cytostatic chemotherapeutic agent)
- IT Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Shiga-like toxin, treatment of effects Shiga-like toxin from E.coli infection; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Interferons
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-proliferative agent; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity for treating hyper-proliferative disorder in combination with addnl. anti-proliferative agent)
- IT Cytotoxic agents
(antimetabolites; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity for treating hyper-proliferative disorder in combination with addnl. cytotoxic agent or cytostatic chemotherapeutic agent)
- IT Fertility
(birth control; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Carcinoma
(bladder, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Skin, disease
(bullous, treatment of bullous disorder associated with subepidermal blister formation; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Bladder, neoplasm
Head, neoplasm
Lung, neoplasm
Mammary gland, neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Prostate gland, neoplasm
Thyroid gland, neoplasm
(carcinoma, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Intestine, neoplasm
(colon, carcinoma, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Carcinoma
Intestine, neoplasm
(colon, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Eye, disease

- (cornea, ulcer, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Ulcer
(corneal, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Thrombosis
(coronary arterial, treatment of coronary thrombosis from atherosclerotic plague; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Artery, disease
(coronary, thrombosis, treatment of coronary thrombosis from atherosclerotic plague; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Cartilage, disease
(degeneration, treatment of degenerative cartilage loss following traumatic joint injury; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Nerve, disease
(demyelination, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enterotoxin A, treatment of effects enterotoxin A from Staphylococcus infection; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Skin, disease
(epidermolysis bullosa, treatment of dystrophobic epidermolysis bullosa; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Carcinoma
(head, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Carcinoma
(hepatocellular, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Liver, neoplasm
(hepatoma, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Eye, disease
(macula, degeneration, treatment of age related macular degeneration; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Carcinoma
(mammary, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Neoplasm
(metastasis, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Microtubule
(microtubule disruptors; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity for treating hyper-proliferative disorder in combination with addnl. cytotoxic agent or cytostatic chemotherapeutic agent)
- IT Hematopoietic precursor cell
(myeloid, treatment of myeloid disorder; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Carcinoma
Neoplasm
(neck, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Neck, anatomical
(neoplasm, carcinoma, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

- IT Neck, anatomical
(neoplasm, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Bone, disease
(osteopenia, treatment of osteopenias mediated by MMP activity; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Carcinoma
(ovarian, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Carcinoma
(pancreatic, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Signal transduction, biological
(preparation of aryl heterocyclyl ureas for treating diseases mediated by the VEGF induced signal transduction pathway)
- IT Angiogenesis
Angiogenesis inhibitors
Anti-infective agents
Antiarthritics
Antirheumatic agents
Antitumor agents
Antiviral agents
Contraceptives
Human
Tuberculostatics
(preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Alkylating agents, biological
(preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity for treating hyper-proliferative disorder in combination with addnl. cytotoxic agent or cytostatic chemotherapeutic agent)
- IT Growth factor receptors
Hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity for treating hyper-proliferative disorder in combination with addnl. cytotoxic agent or cytostatic chemotherapeutic agent)
- IT Carcinoma
(prostatic, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proteinuria, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Carcinoma
(pulmonary, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Kidney, neoplasm
(renal cell carcinoma, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Carcinoma
(renal cell, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Eye, disease
(retinal ischemia, treatment of ischemic retinal-vein occlusion; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)
- IT Ischemia
(retinal, treatment of ischemic retinal-vein occlusion; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

activity)

IT Eye, disease
(retinopathy, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT Arthritis
(septic, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT Neoplasm
(solid, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT Disease, animal
(temporomandibular joint, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT Joint, anatomical
(temporomandibular, disease, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT Carcinoma
(thyroid, treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT Antiulcer agents
(treatment of corneal ulceration; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT Anticoagulants
(treatment of coronary thrombosis from atherosclerotic plague; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT Helicobacter pylori
(treatment of helicobacter pylori infection during peptic ulcer disease; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT Borrelia burgdorferi
Cytomegalovirus
Human immunodeficiency virus
Influenza virus
Theiler's murine encephalomyelitis virus
Treponema pallidum
(treatment of infection from; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT Neisseria meningitidis
(treatment of meningococcal infection; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT Adenoma
Aneurysm
Head, neoplasm
Infection
Kidney, neoplasm
Leukemia
Lung, neoplasm
Mammary gland, neoplasm
Melanoma
Neuroglia, neoplasm
Osteoarthritis
Ovary, neoplasm
Pancreas, neoplasm
Periodontium, disease
Prostate gland, neoplasm
Psoriasis
Rheumatoid arthritis
Stomach, neoplasm
Tuberculosis
(treatment of; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT Vascular endothelial growth factor receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type VEGFR-2; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT 143180-75-0, DNA topoisomerase I

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DNA topoisomerase I inhibitors; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity for treating hyper-proliferative disorder in combination with addnl. cytotoxic agent or cytostatic chemotherapeutic agent)

IT 142805-56-9, DNA topoisomerase II

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DNA topoisomerase II inhibitors; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity for treating hyper-proliferative disorder in combination with addnl. cytotoxic agent)

IT 50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 50-24-8, Prednisolone 50-44-2, 6-Mercaptopurine 50-76-0, Dactinomycin 50-91-9, 5-Fluorodeoxyuridine 51-21-8, 5-Fluorouracil 51-75-2, Mechlorethamine 52-24-4, Thiotepa 53-03-2, Prednisone 53-19-0, Mitotane 55-98-1, Busulfan 56-53-1, Diethylstilbestrol 57-22-7, Vincristine 57-63-6, Ethinyl estradiol 57-85-2, Testosterone propionate 58-05-9, Leucovorin 58-96-8, Uridine 59-05-2, Methotrexate 71-58-9, Medroxyprogesteroneacetate 76-43-7, Fluoxymesterone 125-84-8, Aminogluthethimide 127-07-1, Hydroxyurea 134-46-3, 5-Fluorodeoxyuridine monophosphate 147-94-4, Cytarabine 148-82-3, Melphalan 154-42-7, Thioguanine 154-93-8, Carmustine 305-03-3, Chlorambucil 320-67-2, 5-Azacytidine 446-86-6, Azathioprine 595-33-5, Megestrol acetate 630-56-8, Hydroxyprogesterone caproate 645-05-6, Hexamethylmelamine 671-16-9, Procarbazine 865-21-4, Vinblastine 3778-73-2, Ifosfamide 4291-63-8, Cladribine 4342-03-4, Dacarbazine 9015-68-3, Asparaginase 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 13010-47-4, Lomustine 13311-84-7, Flutamide 13909-09-6, Semustine 15663-27-1, Cisplatin 18378-89-7, Plicamycin 18883-66-4, Streptozocin 19767-45-4, Mesna 20830-81-3, Daunorubicin 23214-92-8, Doxorubicin 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 41575-94-4, Carboplatin 51321-79-0 53643-48-4, Vindesine 53910-25-1, Pentostatin 56420-45-2, Epirubicin 58957-92-9, Idarubicin 61825-94-3, Oxaliplatin 65271-80-9, Mitoxantrone 71486-22-1, Vinorelbine 75607-67-9, Fludarabine phosphate 84449-90-1 95058-81-4, 2',2'-Difluorodeoxycytidine 97682-44-5, Irinotecan 114977-28-5, Docetaxel 123948-87-8, Topotecan 180288-69-1, Herceptin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(anti-proliferative agent; preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity for treating hyper-proliferative disorder in combination with addnl. anti-proliferative agent)

IT 139691-76-2, Raf kinase 150977-45-0, Flk-1 kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)

IT 223724-90-1P	223725-06-2P	223725-07-3P	223725-08-4P	285983-41-7P
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285983-68-8P	285983-70-2P	285983-74-6P	285983-75-7P	285983-76-8P
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294851-56-2P	294851-58-4P	294851-60-8P	294851-62-0P	294851-64-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis
inhibiting activity)

IT	294851-66-4P	294851-68-6P	294851-70-0P	294851-72-2P	294851-74-4P
	294851-76-6P	294855-56-4P	340825-40-3P	340825-41-4P	340825-46-9P
	340825-47-0P	340825-48-1P	340825-49-2P	340825-51-6P	340825-52-7P
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	340825-58-3P	340825-59-4P	477844-71-6P	489432-45-3P	499971-97-0P
	501365-69-1P	585531-85-7P	585531-86-8P	585531-87-9P	585531-88-0P
	585531-89-1P				

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis
inhibiting activity)

IT	368-78-5, 3-Trifluoromethylphenylhydrazine	529-27-1,			
	2-Methylphenylhydrazine	637-60-5, p-Tolylhydrazine hydrochloride			
	1822-51-1, 4-Picolyl chloride hydrochloride	3647-69-6,			
	4-(2-Chloroethyl)morpholine hydrochloride	4900-63-4,			
	4-Methoxy-1-nitronaphthalene	5959-56-8, 4-Amino-1-naphthol hydrochloride			
	6498-34-6, Cyclohexylhydrazine	59997-51-2, 4,4-Dimethyl-3-			
	oxopentanenitrile	63693-65-2, 4-Isopropylphenylhydrazine			
	RL: RCT (Reactant); RACT (Reactant or reagent)				
	(preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis inhibiting activity)				
IT	605-62-9P	285984-22-7P	285984-23-8P	285984-25-0P	317806-88-5P
	317806-90-9P	585531-90-4P			

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis
inhibiting activity)

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD

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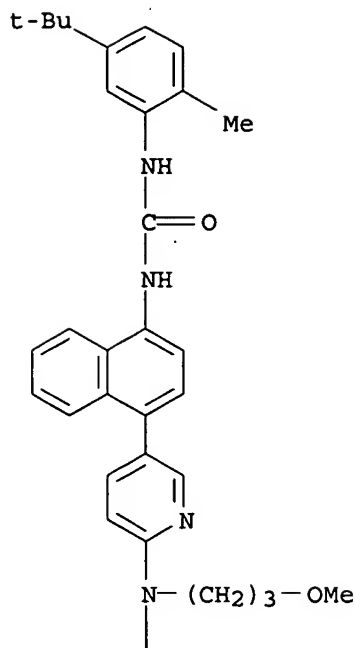
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of aryl heterocyclyl ureas with raf kinase and angiogenesis
inhibiting activity)

RN 294849-86-8 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methylphenyl]-N'-[4-[6-[(3-
methoxypropyl)methylamino]-3-pyridinyl]-1-naphthalenyl]- (9CI) (CA INDEX
NAME)

PAGE 1-A



PAGE 2-A



L24 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2000:666713 HCAPLUS
 DN 133:252426
 ED Entered STN: 22 Sep 2000
 TI Preparation of aromatic heterocyclic ureas as antiinflammatory agents
 IN Betageri, Rajashehar; Breitfelder, Steffen; Cirillo, Pier
 F.; Gilmore, Thomas A.; Hickey, Eugene R.; Kirrane, Thomas
 M.; Moriak, Monica H.; Moss, Neil; Patel, Usha R.;
 Proudfoot, John R.; Regan, John R.; Sharma, Rajiv; Sun,
 Sanxing; Swinamer, Alan D.; Takahashi, Hidenori
 PA Boehringer Ingelheim Pharmaceuticals, Inc., USA
 SO PCT Int. Appl., 282 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07D231-38
 ICS C07D213-38; C07D213-74; A61K031-44; A61K031-50; A61K031-415;
 A61K031-505; C07D401-14; C07D405-12; C07D401-12; C07D213-76;
 C07D409-12; C07D493-08; C07D495-08; A61P029-00; C07D493-08;
 C07D307-00; C07D209-00; C07D495-08; C07D333-00
 CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1
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	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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YU, ZA
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
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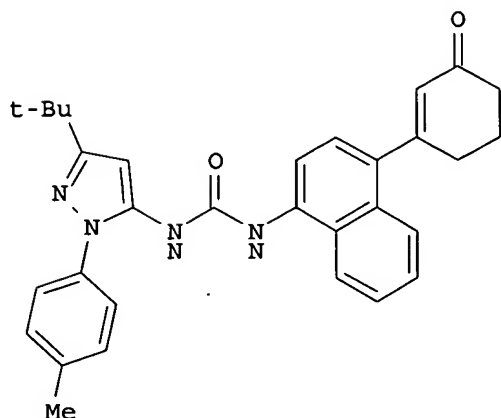
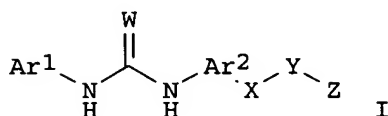
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000055139	ICM ICS	C07D231-38 C07D213-38; C07D213-74; A61K031-44; A61K031-50; A61K031-415; A61K031-505; C07D401-14; C07D405-12; C07D401-12; C07D213-76; C07D409-12; C07D493-08; C07D495-08; A61P029-00; C07D493-08; C07D307-00; C07D209-00; C07D495-08; C07D333-00
EP 1466906	ECLA	C07D213/38; C07D213/74D4; C07D213/76; C07D231/38B3D; C07D401/12+213+209C; C07D401/12+231+213; C07D401/12+241+213; C07D401/12+241B+213; C07D401/14+239B+231+213; C07D405/12+307+213; C07D405/12+307B+231; C07D409/12+335+213; C07D493/08+307B+209B; C07D495/08+333B+209B <--
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US 2002082256 ECLA C07D213/38; C07D401/12+213+211; C07D401/12+231+213;
 C07D401/12+241B+213; C07D401/12+241+213;
 C07D405/12+307+213; C07D405/12+307B+231;
 C07D405/12+309+213; C07D409/12+35+213;
 C07D493/08+307B+209B; C07D495/08+333B+209B;
 C07D213/74D4; C07D213/76; C07D231/38B3D; C07D307/52;
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US 2004019038 ECLA C07D213/38; C07D213/74D4; C07D213/76; C07D231/38B3D;
 C07D307/12; C07D307/52; C07D401/12+213+29C;
 C07D401/12+213+211; C07D401/12+231+213;
 C07D401/12+241B+213; C07D401/12+241+213;
 C07D401/1+239B+231+213; C07D405/12+307+213;
 C07D405/12+307B+231; C07D405/12+309+213;
 C07D409/12+335+213; C07D493/08+307B+209B;
 C07D495/08+333B+209B <--

OS MARPAT 133:252426
 GI



AB The title compds. (I) [wherein Ar1 = (un)substituted pyrrole, pyrrolidine, pyrazole, imidazole, oxazole, thiazole, furan, or thiophene; Ar2 = (un)substituted Ph, (tetrahydro)naphthyl, (tetrahydro)quinoline, (tetrahydro)isoquinoline, benzimidazole, benzofuran, indanyl, indenyl, or indole; W = O or S; X = (un)substituted cycloalkyl, cycloalkenyl, Ph, furan, thiophene, pyrrole, imidazolyl, pyridine, pyrimidine, (dihydro)pyridinone, (dihydro)maleimide, piperidine, piperazine, or pyrazine; Y = a bond or (un)substituted saturated or unsatd. alkyl optionally interrupted by O, NH, S(O), SO2, or S; Z = (un)substituted Ph, pyridine, pyrimidine, pyridazine, imidazole, (tetrahydro)furan, thiophene, (tetrahydro)pyran, 1,3-dioxolanone, 1,3-dioxanone, 1,4-dioxane, (thio)morpholine (sulfoxide), piperidine, cyclohexanone, pentamethylene sulfoxide, etc.] were prepared for the treatment of diseases or pathol. conditions involving inflammation, such as chronic inflammatory diseases. Thus, coupling 2-cyclohexenone with 4-bromo-1-naphthylamine in the presence of Pd(PPh3)2Cl2, DPPP, and NaHCO3 in DMF, followed by conversion of the amine to an isocyanate using ClCOCl and immediate addition of 1-(4-methylphenyl)-3-tert-butyl-1H-pyrazol-5-amine, gave the urea II. In

a cytokine production inhibition assay, preferred compds. of the invention showed IC₅₀ < 10 μ M against TNF- α in lipopolysaccharide stimulated THF cells.

ST arom heterocyclic urea prepn antiinflammatory agent; pyrazolyl arom urea prepn tumor necrosis factor inhibitor; urea arom heterocyclic prepn cytokine inhibitor

IT Anti-inflammatory agents

(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)

IT Tumor necrosis factors

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)

(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)

IT 294851-78-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)

IT	294848-43-4P	294848-46-7P	294848-49-0P	294848-51-4P	294848-53-6P
	294848-55-8P	294848-58-1P	294848-61-6P	294848-64-9P	294848-67-2P
	294848-70-7P	294848-73-0P	294848-76-3P	294848-79-6P	294848-82-1P
	294848-85-4P	294848-88-7P	294848-91-2P	294848-94-5P	294848-96-7P
	294848-98-9P	294849-00-6P	294849-02-8P	294849-04-0P	294849-06-2P
	294849-08-4P	294849-10-8P	294849-12-0P	294849-14-2P	294849-16-4P
	294849-18-6P	294849-20-0P	294849-22-2P	294849-24-4P	294849-26-6P
	294849-28-8P	294849-30-2P	294849-32-4P	294849-34-6P	294849-36-8P
	294849-38-0P	294849-40-4P	294849-42-6P	294849-44-8P	294849-46-0P
	294849-48-2P	294849-50-6P	294849-52-8P	294849-54-0P	294849-56-2P
	294849-58-4P	294849-60-8P	294849-62-0P	294849-64-2P	294849-66-4P
	294849-68-6P	294849-70-0P	294849-72-2P	294849-74-4P	294849-76-6P
	294849-78-8P	294849-80-2P	294849-82-4P	294849-84-6P	
	294849-86-8P	294849-88-0P	294849-90-4P	294849-92-6P	
	294849-94-8P	294849-97-1P	294850-00-3P	294850-02-5P	294850-04-7P
	294850-06-9P	294850-09-2P	294850-12-7P	294850-15-0P	294850-18-3P
	294850-21-8P	294850-24-1P	294850-27-4P	294850-29-6P	294850-31-0P
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	294850-43-4P	294850-45-6P	294850-47-8P	294850-49-0P	294850-51-4P
	294850-53-6P	294850-55-8P	294850-57-0P	294850-59-2P	294850-61-6P
	294850-63-8P	294850-65-0P	294850-67-2P	294850-69-4P	294850-71-8P
	294850-73-0P	294850-76-3P	294850-79-6P	294850-81-0P	294850-84-3P
	294850-87-6P	294850-90-1P	294850-93-4P	294850-96-7P	294850-99-0P
	294851-02-8P	294851-05-1P	294851-07-3P	294851-09-5P	294851-11-9P
	294851-14-2P	294851-16-4P	294851-18-6P	294851-20-0P	294851-22-2P
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	294851-34-6P	294851-36-8P	294851-38-0P	294851-40-4P	294851-42-6P
	294851-44-8P	294851-46-0P	294851-48-2P	294851-50-6P	294851-52-8P
	294851-54-0P	294851-56-2P	294851-58-4P	294851-60-8P	294851-62-0P
	294851-64-2P	294851-66-4P	294851-68-6P	294851-70-0P	294851-72-2P
	294851-74-4P	294851-76-6P	294851-79-9P	294851-81-3P	294851-83-5P
	294851-85-7P	294851-87-9P	294853-11-5P	294855-56-4P	

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)

IT 59-48-3, Oxindole 68-12-2, reactions 75-97-8 95-92-1, Diethyloxalate

109-77-3, Malononitrile 110-91-8, Morpholine, reactions 353-07-1,
 2-Cyanoethylhydrazine 500-22-1, Pyridine-3-carboxaldehyde 585-34-2,
 3-tert-Butylphenol 591-19-5, 3-Bromoaniline 624-28-2,
 2,5-Dibromopyridine 626-35-7, Ethyl nitroacetate 628-22-8,
 3-Cyano-1-propanol 930-68-7, 2-Cyclohexenone 1072-72-6,
 Tetrahydro-1,4-thiopyrone 1072-97-5, 2-Amino-5-bromopyridine
 1445-73-4, 1-Methyl-4-piperidone 1461-22-9, Tributyltin chloride
 1899-24-7, 5-Bromo-2-furaldehyde 2298-07-9, 4-Bromo-1-naphthylamine
 3549-23-3, Methyl 4-tert-butylphenylacetate 4097-49-8, 4-tert-Butyl-2,6-
 dinitrophenol 5292-43-3, tert-Butyl bromoacetate 5414-19-7,
 Bis(2-bromoethyl) ether 6628-77-9, 5-Amino-2-methoxypyridine
 7693-46-1, 4-Nitrophenylchloroformate 29943-42-8, Tetrahydro-4-pyranone
 35944-64-0, 3-Iodo-4-methylphenylamine 59997-51-2, 4,4-Dimethyl-3-
 oxopentanenitrile 62559-08-4, 4-tert-Butyl-2-nitrotoluene 89364-31-8,
 Tetrahydro-3-furoic acid 155959-13-0, 2-tert-Butyl-6-chloro-5-
 methylpyridine-4-carboxylic acid methyl ester 168169-11-7 285984-25-0
 285984-47-6 294853-00-2 294853-07-9 294853-09-1,
 5-tert-Butyl-2-methoxyphenylacetic acid

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of aromatic heterocyclic urea antiinflammatory agents by
 conversion of arylamines to isocyanates followed by addition of
 heterocyclic amines)

IT 1914-02-9P 4210-60-0P 6309-59-7P 14011-21-3P 16078-32-3P
 19155-24-9P 21905-78-2P 21926-00-1P 29682-15-3P 31181-90-5P
 32857-63-9P 71897-83-1P 72934-84-0P 79710-86-4P 83405-70-3P
 88905-15-1P 99170-18-0P 116584-61-3P 116584-62-4P 160664-95-9P
 197846-82-5P 229003-11-6P 261711-84-6P 294851-89-1P 294851-91-5P
 294851-93-7P 294851-95-9P 294851-97-1P 294851-99-3P 294852-01-0P
 294852-03-2P 294852-05-4P 294852-07-6P 294852-09-8P 294852-12-3P
 294852-14-5P 294852-18-9P 294852-20-3P 294852-22-5P 294852-24-7P
 294852-26-9P 294852-28-1P 294852-30-5P 294852-32-7P 294852-35-0P
 294852-37-2P 294852-39-4P 294852-41-8P 294852-43-0P 294852-45-2P
 294852-47-4P 294852-49-6P 294852-50-9P 294852-52-1P 294852-54-3P
 294852-59-8P 294852-61-2P 294852-64-5P 294852-66-7P 294852-68-9P
 294852-70-3P 294852-71-4P 294852-73-6P 294852-75-8P 294852-76-9P
 294852-78-1P 294852-80-5P 294852-82-7P 294852-84-9P 294852-86-1P
 294852-88-3P 294852-90-7P 294852-92-9P 294852-94-1P 294852-96-3P
 294852-98-5P 294853-13-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation of aromatic heterocyclic urea antiinflammatory agents by
 conversion of arylamines to isocyanates followed by addition of
 heterocyclic amines)

IT 294849-86-8P

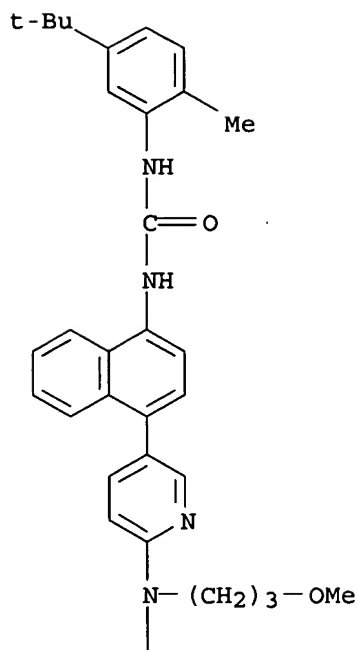
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aromatic heterocyclic urea antiinflammatory agents by
 conversion of arylamines to isocyanates followed by addition of
 heterocyclic amines)

RN 294849-86-8 HCAPLUS

CN Urea, N-[5-(1,1-dimethylethyl)-2-methylphenyl]-N'-[4-[6-[(3-
 methoxypropyl)methylamino]-3-pyridinyl]-1-naphthalenyl]- (9CI) (CA INDEX
 NAME)

PAGE 1-A



PAGE 2-A



=> => fil reg

FILE 'REGISTRY' ENTERED AT 10:23:42 ON 14 MAR 2005

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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STRUCTURE FILE UPDATES: 13 MAR 2005 HIGHEST RN 845467-46-1

DICTIONARY FILE UPDATES: 13 MAR 2005 HIGHEST RN 845467-46-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

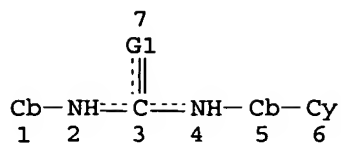
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d sta que 160

L25 STR



VAR G1=O/S

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 7

STEREO ATTRIBUTES: NONE

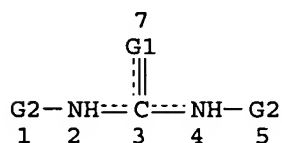
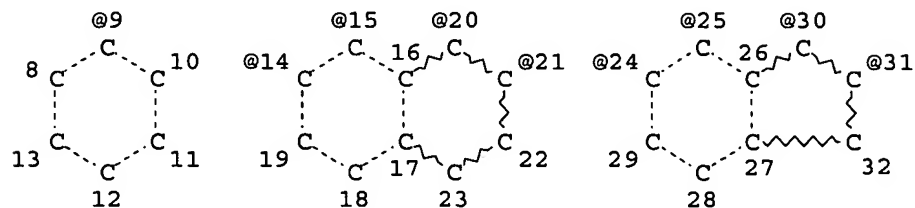
L27 SCR 1454 AND 1840 AND 1993

L28 SCR 2039 OR 2050 OR 2049 OR 2048 OR 2053 OR 2052 OR 2051 O

R 2043 OR 2054 OR 1918

L30 9410 SEA FILE=REGISTRY SSS FUL L25 AND L27 NOT L28

L49 STR



VAR G1=O/S

VAR G2=9/14/15/20/21/24/25/30/31

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

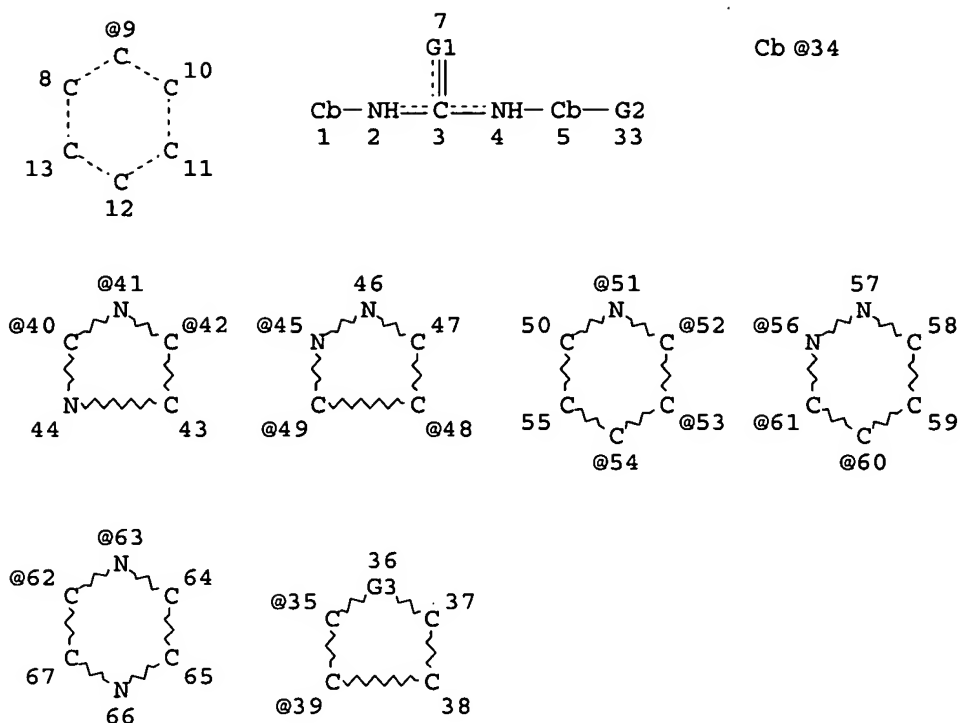
RSPEC 8 14 24

NUMBER OF NODES IS 31

STEREO ATTRIBUTES: NONE

L51 8739 SEA FILE=REGISTRY SUB=L30 SSS FUL L49

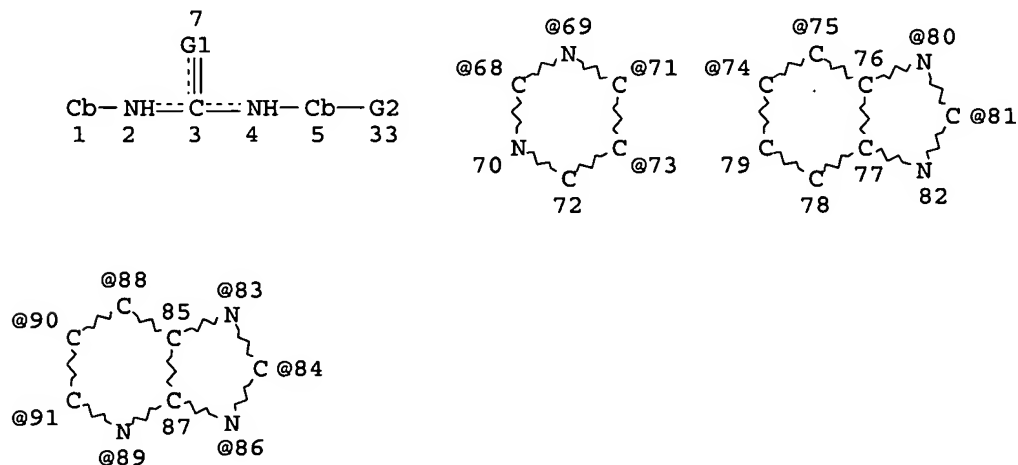
L57 STR



VAR G1=O/S
 VAR G2=34/9/35/39/40/41/42/45/49/48/51/52/53/54/56/61/60/63/62
 VAR G3=O/S/N
 NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED
 ECOUNT IS M3-X8 C AT 34

GRAPH ATTRIBUTES:
 RSPEC I
 NUMBER OF NODES IS 47

STEREO ATTRIBUTES: NONE
 L58 STR



VAR G1=O/S

VAR G2=68/69/71/73/80/81/75/74/83/84/86/89/91/90/88

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 31

STEREO ATTRIBUTES: NONE

L60 3402 SEA FILE=REGISTRY SUB=L51 SSS FUL (L57 OR L58)

100.0% PROCESSED 8739 ITERATIONS

3402 ANSWERS

SEARCH TIME: 00.00.01

=> d his

(FILE 'HOME' ENTERED AT 08:52:21 ON 14 MAR 2005)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 08:52:37 ON 14 MAR 2005

L1 3 S (US20040019038 OR US6660732 OR US20020055507 OR US6656933 OR
E CIRILLO P/AU
L2 48 S E3,E6-E8
E BREITFELDER S/AU
L3 19 S E5,E6
E PATEL U/AU
L4 58 S E3,E12,E37,E41,E42
E PROUDFOOT J/AU
L5 261 S E3,E5,E7-E9
E SWINAMER A/AU
L6 9 S E4-E6
E TAKAHASHI H/AU
L7 1739 S E3-E8,E95-E97
E GILMORE T/ AU
L8 44 S E3,E4,E11,E12,E21
E SHARMA R/AU
L9 3007 S E3-E26,E94-E97
E BOHRING/PA,CS
L10 10 S E3-E12
E BOEHRING/PA,CS
E BOEHRING/PA,CS
L11 8534 S BOEHRING?/PA,CS
L12 3 S L1 AND L2-L11
SEL RN

FILE 'REGISTRY' ENTERED AT 08:59:15 ON 14 MAR 2005

L13 347 S E1-E347
L14 151 S L13 AND 46.150.18/RID AND C6-C6/ES AND NC5/ES
L15 8 S L14 AND 4/NR
L16 1 S L15 AND C32H38N4O2
L17 0 S 294849-86-8/CRN
E C32H38N4O2/MF
L18 1 S E3 AND 46.150.18/RID AND C6-C6/ES AND NC5/ES
L19 1 S L16,L18

FILE 'HCAOLD' ENTERED AT 09:02:13 ON 14 MAR 2005

L20 0 S L19

FILE 'USPATFULL' ENTERED AT 09:02:14 ON 14 MAR 2005

L21 6 S L19

FILE 'HCAPLUS' ENTERED AT 09:02:35 ON 14 MAR 2005

L22 2 S L19
L23 1 S L22 AND L1-L12
L24 2 S L22,L23

FILE 'REGISTRY' ENTERED AT 09:03:00 ON 14 MAR 2005

FILE 'USPATFULL' ENTERED AT 09:03:07 ON 14 MAR 2005

FILE 'HCAPLUS' ENTERED AT 09:03:15 ON 14 MAR 2005

FILE 'REGISTRY' ENTERED AT 09:03:32 ON 14 MAR 2005

L25 STR
L26 7 S L25
L27 SCR 1454 AND 1840 AND 1993
L28 SCR 2039 OR 2050 OR 2049 OR 2048 OR 2053 OR 2052 OR 2051 OR 204
L29 44 S L25 AND L27 NOT L28 SAM
L30 9410 S L25 AND L27 NOT L28 FUL
SAV L30 ZINNA624/A TEMP
L31 103 S C10H8/MF AND C6-C6/ES
L32 48 S L31 NOT (D OR T)/ELS
L33 12 S L32 AND DIHYDRO?
L34 7 S L33 NOT (IUM OR ION)
E 591.49/RID
L35 603 S L30 AND E3
E TETRAHYDRONAPHTH?/CN
L36 1 S E4
E NAPHTHALENE/CN
L37 1 S E3
L38 9352 S 46.150.18/RID AND L30
E BENZOCYCLOBUTANE/CN
L39 1 S E3
L40 0 S 191.7/RID AND L30
L41 4 S C4-C6/ES AND L30
E BENZOCYCLOHEPTANE/CN
L42 1 S E3
L43 2 S E9
L44 0 S C6-C7/ES AND L30
E INDANECN
E INDANE/CN
L45 2 S E3
L46 50 S 333.70/RID AND L30
L47 50 S C5-C6/ES AND L30
E INDENE/CN
L48 1 S E3
L49 STR L25
L50 50 S L49 SAM SUB=L30
L51 8739 S L49 FUL SUB=L30
SAV TEMP L51 ZINNA624A/A
L52 135 S L13 AND L51
L53 134 S L52 NOT L19
L54 8604 S L51 NOT L52
E 3H-IMIDAZOL/CN
E "3H-IMIDAZO[4,5-B]PYRIDINE"/CN
E "3H-IMIDAZO(4,5-B)PYRIDINE"/CN
L55 2 S E3
L56 STR L49
L57 STR L56
L58 STR L56
L59 50 S (L57 OR L58) SAM SUB=L51
L60 3402 S (L57 OR L58) FUL SUB=L51
SAV L60 TEMP ZINNA624B/A

L61 135 S L60 AND L52
L62 3267 S L60 NOT L61
L63 134 S L61 AND L53

FILE 'HCAOLD' ENTERED AT 09:46:45 ON 14 MAR 2005

L64 0 S L63

FILE 'HCAPLUS' ENTERED AT 09:47:05 ON 14 MAR 2005

L65 9 S L63
L66 8 S L65 AND L1-L12
L67 2 S L65,L66 AND (PD<=19990312 OR PRD<=19990312 OR AD<=19999312)
L68 576 S L62
L69 444 S L68 AND (PD<=19990312 OR PRD<=19990312 OR AD<=19999312)
E INFLAMMATION/CT
L70 20 S E3-E22,E25 AND L69
E E3+ALL
L71 19 S E2+NT AND L69
E E40+ALL
L72 12 S E4,E5 AND L69
L73 28 S E3,E11-E17 AND L69
L74 43 S L70-L73
L75 38 S L69 AND ?INFLAM?
E TUMOR NECROSIS FACTOR/CT
E E78+ALL
L76 5 S E3,E4,E2+NT AND L69
E E22+ALL
L77 1 S E12-E15,E11+NT AND L69
L78 1 S (TNFALFA OR TNFALPHA OR ALFATNF OR ALPHATNF OR (ALFA OR ALPHA
L79 5 S (TNF OR TUMOR NECROSIS FACTOR) AND L69
L80 44 S L74-L79
L81 211 S L62(L) (THU OR PAC OR PKT OR DMA)/RL
L82 97 S L69 AND L81
L83 31 S L80 AND L82
L84 44 S L80 AND P/DT
L85 42 S L84 AND US/PC,PRC,AC
L86 37 S L84 AND US/PC.B,PRC.B,AC.B
L87 27 S L83 AND L86
L88 17 S L80,L83-L86 NOT L87
L89 44 S L87,L88 AND L68-L88
SEL HIT RN

FILE 'REGISTRY' ENTERED AT 09:56:50 ON 14 MAR 2005

L90 153 S E1-E153
L91 8 S L90 AND (C24H24CL2N2O2 OR C25H28N2O2 OR C24H24F2N2O2 OR C23H2

FILE 'HCAPLUS' ENTERED AT 10:23:06 ON 14 MAR 2005

L92 2 S L91
L93 4 S L67,L92

FILE 'REGISTRY' ENTERED AT 10:23:42 ON 14 MAR 2005

=> fil hcaplus

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FILE COVERS 1907 - 14 Mar 2005 VOL 142 ISS 12
FILE LAST UPDATED: 13 Mar 2005 (20050313/ED)

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L92 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:433797 HCAPLUS
DN 140:423477
ED Entered STN: 28 May 2004
TI Preparation of diaryl ureas as inhibitors of p38 kinase
IN Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy B.; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David E.; Hatoum-Mokdad, Holia; Rodriguez, Marell; Sibley, Robert; Wang, Ming; Turner, Tiffany; Brennan, Catherine
PA Bayer Corporation, USA
SO U.S. Pat. Appl. Publ., 60 pp., Cont. of U.S. Ser. No. 458,015, abandoned.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-44
ICS A61K031-381; A61K031-325; A61K031-277; A61K031-17; A61K031-216; A61K031-195
NCL 546306000; 549069000; 558418000; 560024000; 564050000; 564049000; 514349000; 514447000; 514485000; 514522000
CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 27, 28, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004102636	A1	20040527	US 2002-60396	20020201
PRAI	US 1997-126439P	P	19971222		
	US 1998-285522	B1	19981222		
	US 1999-458015	B1	19991210		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004102636	ICM	A61K031-44
	ICS	A61K031-381; A61K031-325; A61K031-277; A61K031-17; A61K031-216; A61K031-195
	NCL	546306000; 549069000; 558418000; 560024000; 564050000; 564049000; 514349000; 514447000; 514485000; 514522000

OS MARPAT 140:423477

AB A method of treating a p-38 mediated disease other than cancer comprises administration of BNHCONHA [A = (substituted) Ph, pyridyl, 2-thienyl; B = (substituted) aryl, heteroaryl containing ≥ 1 6-membered aromatic structure containing 0-4 N, O, or S atoms]. Thus, 5-tert-butyl-2-(3-tetrahydrofuranyloxy)aniline (preparation given) and p-tolyl isocyanate were stirred 8 h in PhMe to give 75% N-(5-tert-butyl-2-(3-tetrahydrofuranyloxy)phenyl)-N'-(4-methylphenyl)urea. Title compds. inhibited p38 kinase with IC₅₀ = 1-10 μ M.

ST urea diaryl prepn p38 protein kinase inhibitor

IT Transplant and Transplantation

(host-vs.-graft reaction; preparation of diaryl ureas as inhibitors for treating diseases mediated by a cytokine or protease regulated by p38)

IT Intestine, disease
(inflammatory; preparation of diaryl ureas as inhibitors for treating diseases mediated by a cytokine or protease regulated by p38)

IT Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antirheumatic agents
Asthma
Human
Immunity
Immunomodulators
Inflammation
Osteoarthritis
Osteoporosis
Rheumatoid arthritis
(preparation of diaryl ureas as inhibitors for treating diseases mediated by a cytokine or protease regulated by p38)

IT Interleukin 1
Interleukin 6
Interleukin 8
Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of diaryl ureas as inhibitors for treating diseases mediated by a cytokine or protease regulated by p38)

IT Shock (circulatory collapse)
(septic; preparation of diaryl ureas as inhibitors for treating diseases mediated by a cytokine or protease regulated by p38)

IT 165245-96-5, p38 Kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of diaryl ureas as inhibitors of p38 kinase)

IT 9001-12-1, MMP-1 79955-99-0, MMP-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of diaryl ureas as inhibitors for treating diseases mediated by a cytokine or protease regulated by p38)

IT 228416-78-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of diaryl ureas as inhibitors of p38 kinase)

IT 370-50-3P 117745-34-3P 228399-32-4P 228399-33-5P 228399-34-6P
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 228418-42-6P 228418-48-2P 228418-49-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of diaryl ureas as inhibitors of p38 kinase)

IT 86-84-0, 1-Naphthyl isocyanate 96-49-1, Ethylene carbonate 100-11-8,
 4-Nitrobenzyl bromide 100-15-2, N-Methyl-4-nitroaniline 101-77-9
 106-44-5, reactions 106-49-0, p-Toluidine, reactions 108-30-5,
 reactions 109-00-2, 3-Hydroxypyridine 110-91-8, Morpholine, reactions
 123-30-8, 4-Aminophenol 150-76-5, 4-Methoxyphenol 288-32-4, Imidazole,
 reactions 320-94-5, 2-Nitro-4-trifluoromethylbenzoic acid 327-78-6
 349-65-5, 2-Methoxy-5-trifluoromethylaniline 350-46-9,
 1-Fluoro-4-nitrobenzene 371-40-4, 4-Fluoroaniline 400-74-8,
 2-Fluoro-5-nitrobenzotrifluoride 452-80-2, 2-Fluoro-4-methylaniline
 453-20-3, 3-Hydroxytetrahydrofuran 498-74-8 542-69-8, 1-Iodobutane
 551-06-4, 1-Naphthyl isothiocyanate 585-34-2, m-tert-Butylphenol
 585-79-5, 1-Bromo-3-nitrobenzene 598-21-0, Bromoacetyl bromide
 620-95-1, 3-Benzylpyridine 622-58-2, p-Tolyl isocyanate 624-28-2,
 2,5-Dibromopyridine 626-61-9, 4-Chloropyridine 673-09-6 768-35-4
 872-31-1, 3-Bromothiophene 883-99-8, Methyl 3-hydroxy-2-naphthoate
 1083-48-3, 4-(4-Nitrobenzyl)pyridine 1121-78-4, 5-Hydroxy-2-
 methylpyridine 1849-36-1 2033-89-8, 3,4-Dimethoxyphenol 2103-88-0,
 2-Mercapto-4-phenylthiazole 3279-07-0, 4-tert-Butyl-2-nitrophenol
 3535-88-4, 5-tert-Butyl-2-methoxyaniline 3678-63-5 4548-45-2,
 2-Chloro-5-nitropyridine 4556-23-4, 4-Mercaptopyridine 4595-59-9,
 5-Bromopyrimidine 6310-19-6, 4-tert-Butyl-2-nitroaniline 6358-07-2
 7379-35-3, 4-Chloropyridine hydrochloride 21101-60-0,
 4-(4-Nitrophenylthio)phenol 22948-02-3, 3-Aminothiophenol 29264-35-5
 36265-31-3 59669-59-9, 5-Amino-3-tert-butylisoxazole 73322-01-7
 198077-72-4 228401-47-6 228401-48-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of diaryl ureas as inhibitors of p38 kinase)

IT 726-17-0P 780-90-5P 843-06-1P 883-62-5P 885-87-0P 5651-77-4P
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 36089-89-1P 40299-87-4P 51834-97-0P 61500-87-6P 62248-47-9P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation of diaryl ureas as inhibitors of p38 kinase)

IT 228417-60-5P 228417-62-7P 228417-63-8P
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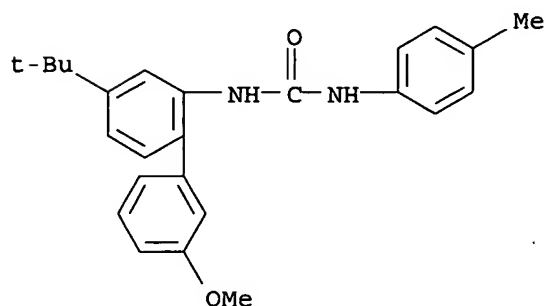
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses).

(preparation of diaryl ureas as inhibitors of p38 kinase)

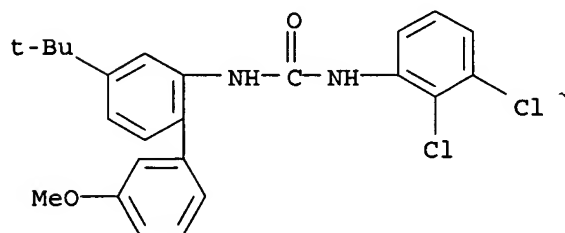
RN 228417-60-5 HCAPLUS

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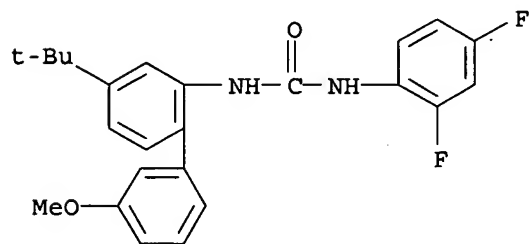
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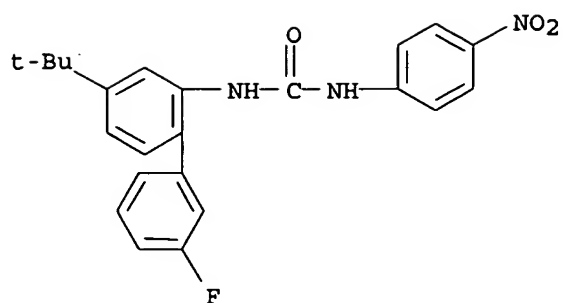
RN 228417-63-8 HCAPLUS

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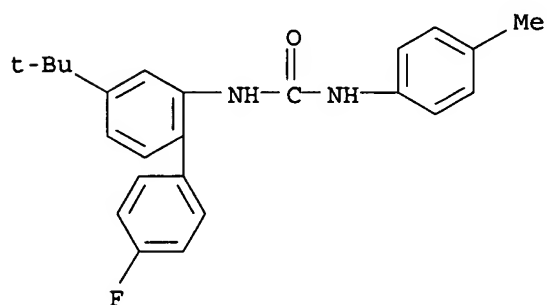
RN 228417-64-9 HCAPLUS

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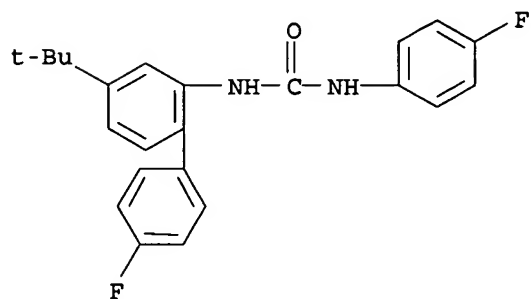
RN 228417-65-0 HCAPLUS

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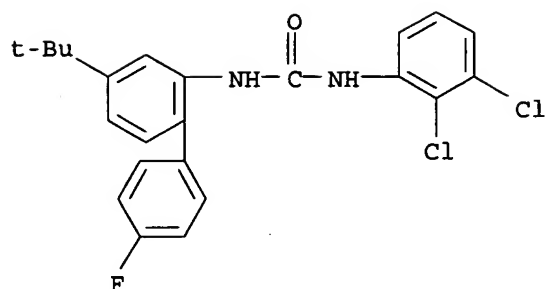
RN 228417-66-1 HCAPLUS

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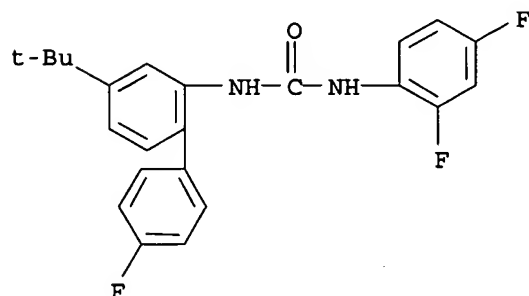
RN 228417-67-2 HCAPLUS

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RN 228417-68-3 HCAPLUS

CN Urea, N-(2,4-difluorophenyl)-N'-[4-(1,1-dimethylethyl)-4'-fluoro[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



L92 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:421667 HCAPLUS

DN 131:58659

ED Entered STN: 08 Jul 1999

TI Preparation of diaryl ureas as inhibitors of p38 kinase.

IN Miller, Scott; Osterhout, Martin; Dumas, Jacques; Khire, Uday; Lowinger, Timothy Bruno; Riedl, Bernd; Scott, William J.; Smith, Roger A.; Wood, Jill E.; Gunn, David; Hatoum-Mokdad, Holia; Rodriguez, Mareli; Sibley, Robert; Wang, Ming

PA Bayer Corporation, USA

SO PCT Int. Appl., 107 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07D273-00

ICS C07D275-00; A61K031-17

CC 25-21 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 1, 27, 28

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9932463	A1	19990701	WO 1998-US27265	19981222
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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AU 9919399	A1	19990712	AU 1999-19399	19981222
EP 1042305	A1	20001011	EP 1998-964221	19981222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001526276	T2	20011218	JP 2000-525400	19981222
PRAI US 1997-995749	A	19971222		
WO 1998-US27265	W	19981222		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9932463	ICM	C07D273-00
	ICS	C07D275-00; A61K031-17
WO 9932463	ECLA	A61K031/17; A61K031/4402; A61K031/4406; A61K031/4409; A61K031/4436; A61K031/4439; A61K031/535P; C07C275/30; C07C275/34; C07C275/36; C07C309/88; C07C311/48; C07C317/42; C07D207/26B2; C07D207/26C; C07D207/26L; C07D207/40B; C07D209/76; C07D209/88; C07D213/40L; C07D213/53B; C07D213/70D; C07D231/08; C07D233/22; C07D233/70; C07D277/68B; C07D307/20; C07D333/0; C07D409/12+333B+213; A61K031/403; A61K031/4035; A61K031/428; A61K031/44+A

OS MARPAT 131:58659

AB A method of treating a p-38 mediated disease other than cancer comprises administration of BNHCONHA [A = (substituted) Ph, pyridyl, 2-thienyl; B = (substituted) aryl, heteroaryl containing ≥ 1 6-membered aromatic structure containing 0-4 N, O, or S atoms]. Thus, 5-tert-butyl-2-(3-tetrahydrofuranyloxy)aniline (preparation given) and p-tolyl isocyanate were stirred 8 h in PhMe to give 75% N-(5-tert-butyl-2-(3-tetrahydrofuranyloxy)phenyl)-N'-(4-methylphenyl)urea. Title compds. inhibited p38 kinase with IC₅₀ = 1-10 μ M.

ST urea diaryl prepn protein kinase inhibitor

IT 165245-96-5, p38 Kinase

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(inhibitors; preparation of diaryl ureas as inhibitors of p38 kinase)

IT 228416-78-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of diaryl ureas as inhibitors of p38 kinase)

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	228417-67-2P	228417-68-3P	228417-69-4P	228417-70-7P	

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 228418-39-1P 228418-40-4P 228418-41-5P 228418-42-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diaryl ureas as inhibitors of p38 kinase)

IT 228399-41-5 228418-48-2 228418-49-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of diaryl ureas as inhibitors of p38 kinase)

IT 86-84-0, 1-Naphthyl isocyanate 96-49-1, Ethylene carbonate 100-11-8, 4-Nitrobenzyl bromide 100-15-2, N-Methyl-4-nitroaniline 101-77-9 106-44-5, reactions 106-49-0, p-Toluidine, reactions 108-30-5, reactions 109-00-2, 3-Hydroxypyridine 110-91-8, Morpholine, reactions 123-30-8, 4-Aminophenol 150-76-5, 4-Methoxyphenol 288-32-4, Imidazole, reactions 320-94-5, 2-Nitro-4-trifluoromethylbenzoic acid 327-78-6 349-65-5, 2-Methoxy-5-trifluoromethylaniline 350-46-9, 1-Fluoro-4-nitrobenzene 371-40-4, 4-Fluoroaniline 400-74-8, 2-Fluoro-5-nitrobenzotrifluoride 452-80-2, 2-Fluoro-4-methylaniline 453-20-3, 3-Hydroxytetrahydrofuran 498-74-8 542-69-8, 1-Iodobutane 551-06-4, 1-Naphthyl isothiocyanate 585-34-2, m-tert-Butylphenol 585-79-5, 1-Bromo-3-nitrobenzene 598-21-0, Bromoacetyl bromide 620-95-1, 3-Benzylpyridine 622-58-2, p-Tolyl isocyanate 624-28-2, 2,5-Dibromopyridine 626-61-9, 4-Chloropyridine 673-09-6 768-35-4 872-31-1, 3-Bromothiophene 883-99-8, Methyl 3-hydroxy-2-naphthoate 1083-48-3, 4-(4-Nitrobenzyl)pyridine 1121-78-4, 5-Hydroxy-2-methylpyridine 1849-36-1 2033-89-8, 3,4-Dimethoxyphenol 2103-88-0, 2-Mercapto-4-phenylthiazole 3279-07-0, 4-tert-Butyl-2-nitrophenol 3535-88-4, 5-tert-Butyl-2-methoxyaniline 3678-63-5 4548-45-2, 2-Chloro-5-nitropyridine 4556-23-4, 4-Mercaptopyridine 4595-59-9, 5-Bromopyrimidine 6310-19-6, 4-tert-Butyl-2-nitroaniline 6358-07-2 7379-35-3, 4-Chloropyridine hydrochloride 21101-60-0, 4-(4-Nitrophenylthio)phenol 22948-02-3, 3-Aminothiophenol 29264-35-5 36265-31-3 59669-59-9, 5-Amino-3-tert-butylisoxazole 73322-01-7 198077-72-4 228401-47-6 228401-48-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of diaryl ureas as inhibitors of p38 kinase)

IT 726-17-0P 780-90-5P 843-06-1P 883-62-5P 885-87-0P 5651-77-4P 6337-24-2P 13041-60-6P 13472-85-0P 16588-75-3P 18994-90-6P 27692-74-6P 28232-34-0P 28232-52-2P 31465-36-8P 32361-76-5P 36089-89-1P 40299-87-4P 51834-97-0P 61500-87-6P 62248-47-9P 62248-51-5P 64064-63-7P 67291-63-8P 70991-08-1P 92575-23-0P 116289-71-5P 135680-03-4P 142596-52-9P 178809-75-1P 220000-87-3P 228401-08-9P 228401-09-0P 228401-10-3P 228401-11-4P 228401-14-7P 228401-15-8P 228401-16-9P 228401-17-0P 228401-18-1P 228401-19-2P 228401-20-5P 228401-21-6P 228401-23-8P 228401-24-9P 228401-26-1P 228401-27-2P 228401-28-3P 228401-29-4P 228401-31-8P 228401-32-9P 228401-33-0P 228401-34-1P 228401-35-2P 228401-36-3P 228401-37-4P 228401-38-5P 228401-39-6P 228401-40-9P 228401-41-0P 228401-43-2P 228401-44-3P 228401-45-4P 228418-45-9P 228418-46-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation of diaryl ureas as inhibitors of p38 kinase)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Frick; US 3230141 1966
- (2) Geigy, J; GB 0828231 A 1960 HCAPLUS
- (3) Kabbe; US 4405644 A 1983 HCAPLUS
- (4) Martin; US 3151023 A 1964
- (5) Martin; US 3200035 A 1965

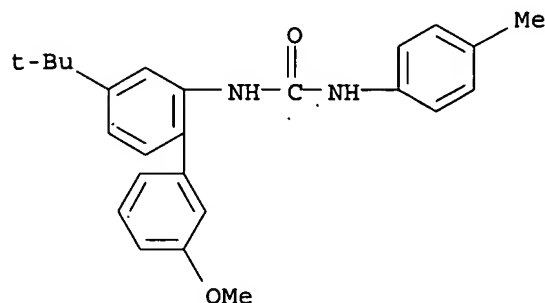
IT 228417-60-5P 228417-62-7P 228417-63-8P
 228417-64-9P 228417-65-0P 228417-66-1P
 228417-67-2P 228417-68-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diaryl ureas as inhibitors of p38 kinase)

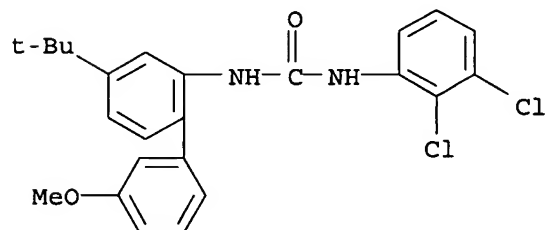
RN 228417-60-5 HCAPLUS

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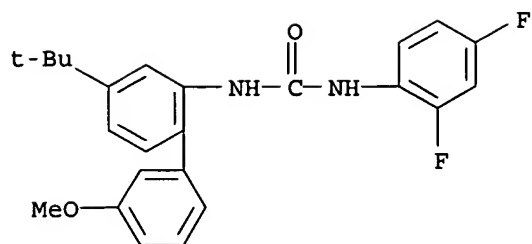
RN 228417-62-7 HCAPLUS

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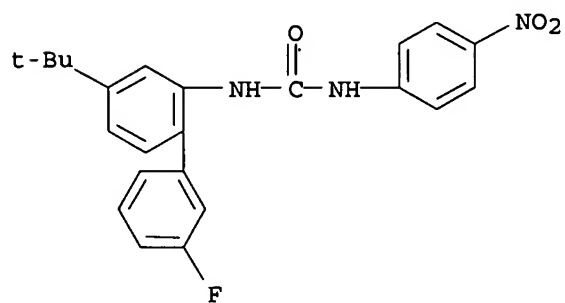
RN 228417-63-8 HCAPLUS

CN Urea, N-(2,4-difluorophenyl)-N'-[4-(1,1-dimethylethyl)-3'-methoxy[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



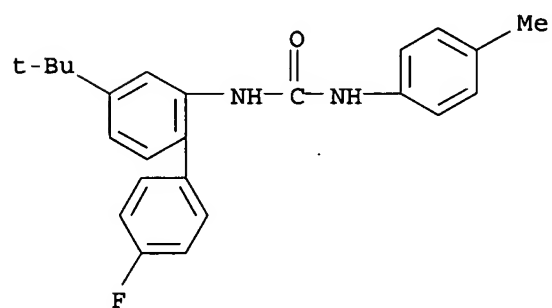
RN 228417-64-9 HCAPLUS

CN Urea, N-[4-(1,1-dimethylethyl)-3'-fluoro[1,1'-biphenyl]-2-yl]-N'-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



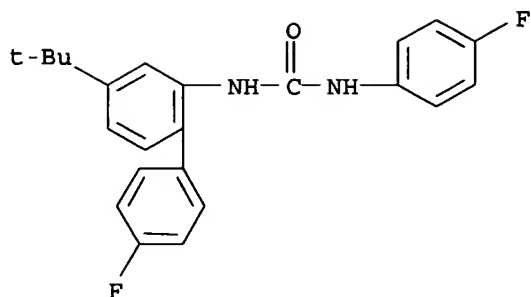
RN 228417-65-0 HCAPLUS

CN Urea, N-[4-(1,1-dimethylethyl)-4'-fluoro[1,1'-biphenyl]-2-yl]-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



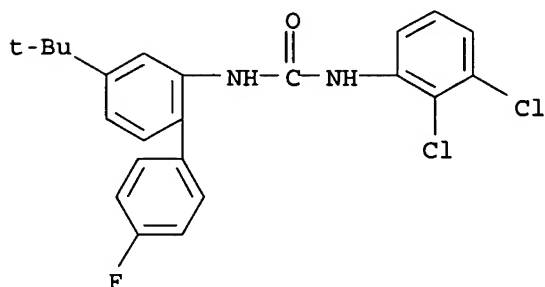
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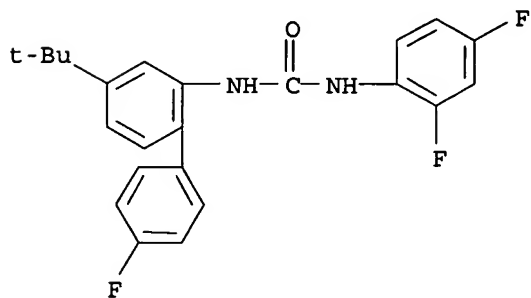
RN 228417-67-2 HCAPLUS

CN Urea, N-(2,3-dichlorophenyl)-N'-[4-(1,1-dimethylethyl)-4'-fluoro[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



RN 228417-68-3 HCAPLUS

CN Urea, N-(2,4-difluorophenyl)-N'-[4-(1,1-dimethylethyl)-4'-fluoro[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



=> d 167 all fhitr tot

L67 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:185696 HCAPLUS

DN 136:247592

ED Entered STN: 15 Mar 2002

TI Preparation of heterocyclyl arylamides and ureas as antiinflammatory agents

IN Breitfelder, Steffen; Cirillo, Pier F.; Regan, John R.

PA Germany

SO U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 505,582.
CODEN: USXXCO

DT Patent
 LA English
 IC ICM A61K031-5377
 ICS C07D413-02
 NCL 514227800
 CC 28-13 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002032195	A1	20020314	US 2001-834797	20010413 <--
	US 6608052	B2	20030819		
	US 6358945	B1	20020319	US 2000-505582	20000216 <--
	US 2002055507	A1	20020509	US 2001-962709	20010925 <--
	US 6660732	B2	20031209		
	US 2002082256	A1	20020627	US 2001-962057	20010925 <--
	US 6656933	B2	20031202		
	US 2003065034	A1	20030403	US 2002-264689	20021004 <--
	US 6703525	B2	20040309		
	US 2003225077	A1	20031204	US 2003-424613	20030428 <--
	US 2004019038	A1	20040129	US 2003-624289	20030721 <--
PRAI	US 2000-505582	A2	20000216	<--	
	US 1999-124148P	P	19990312	<--	
	US 1999-165867P	P	19991116	<--	
	US 2001-834797	A2	20010413		
	US 2001-962057	A1	20010925	<--	
	US 2001-962709	A3	20010925	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2002032195	ICM ICS NCL	A61K031-5377 C07D413-02 514227800
US 2002032195	ECLA	C07D213/38; C07D307/12; C07D307/52; C07D401/12+213+211; C07D405/12+309+213; C07D409/12+335+213 <--
US 6358945	ECLA	C07D213/38; C07D213/74D4; C07D213/76; C07D231/38B3D; C07D307/12; C07D307/52; C07D401/12+213+29C; C07D401/12+213+211; C07D401/12+231+213; C07D401/12+241B+213; C07D401/12+241+213; C07D401/1+239B+231+213; C07D405/12+307+213; C07D405/12+307B+231; C07D405/12+309+213; C07D409/12+335+213; C07D493/08+307B+209B; C07D495/08+333B+209B <--
US 2002055507	ECLA	C07D213/38; C07D213/74D4; C07D213/76; C07D231/38B3D; C07D307/12; C07D307/52; C07D401/12+213+29C; C07D401/12+213+211; C07D401/12+231+213; C07D401/12+241B+213; C07D401/12+241+213; C07D401/1+239B+231+213; C07D405/12+307+213; C07D405/12+307B+231; C07D405/12+309+213; C07D409/12+335+213; C07D493/08+307B+209B; C07D495/08+333B+209B <--
US 2002082256	ECLA	C07D213/38; C07D401/12+213+211; C07D401/12+231+213; C07D401/12+241B+213; C07D401/12+241+213; C07D405/12+307+213; C07D405/12+307B+231; C07D405/12+309+213; C07D409/12+35+213; C07D493/08+307B+209B; C07D495/08+333B+209B; C07D213/74D4; C07D213/76; C07D231/38B3D; C07D307/52; C07D401/12+213+209C <--
US 2003065034	ECLA	C07D213/38; C07D307/12; C07D307/52; C07D401/12+213+211; C07D405/12+309+213; C07D409/12+335+213 <--
US 2004019038	ECLA	C07D213/38; C07D213/74D4; C07D213/76; C07D231/38B3D; C07D307/12; C07D307/52; C07D401/12+213+29C; C07D401/12+213+211; C07D401/12+231+213;

C07D401/12+241B+213; C07D401/12+241+213;
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 C07D405/12+307B+231; C07D405/12+309+213;
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 C07D495/08+333B+209B

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OS MARPAT 136:247592

AB GEC(:W)NHArXYZ [E = O, NH, S; G = (substituted) Ph, naphthyl, benzocyclobutyl, dihydronaphthyl, benzocycloheptyl, indanyl, indenyl, pyridyl, quinolinyl, oxetanyl, pyrrolidinyl, piperidinyl, etc.; Ar = (substituted) Ph, naphthyl, quinolinyl, isoquinolinyl, tetrahydronaphthyl, benzofuryl, benzothienyl, benzimidazolyl, indanyl, etc.; X = (substituted) cycloalkyl, cycloalkenyl, aryl, furyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, pyridinyl, etc.; Y = bond, (substituted) (O-, S-, SO-, SO2-, N-interrupted) alkylene; Z = (substituted) pyridinyl, piperazinyl, pyrimidinyl, pyrazinyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, furyl, thienyl, etc.; W = O, S], were prepared Thus, 5-tert-butyl-2-methoxy-1,3-dinitrobenzene (preparation given) was stirred with ammonium formate and Pd/C in EtOH followed by 3 h reflux to give 90% diamine, which in MeOH was treated with 3,4-dimethoxycyclobutene-1,2-dione at 0-5° followed by stirring and warming to room temperature to give an intermediate. The intermediate in THF was treated with Me2NH at 0-5° followed by stirring and warming to room temperature to give the dimethylamino intermediate.

The latter in CH2Cl2 was treated with COCl2 in PhMe and aqueous NaHCO3 followed by removal of most volatiles. The residue was added to 1-amino-4-(6-morpholin-4-ylmethylpyridin-3-yl)naphthalene (preparation given) in THF followed by stirring overnight to give 1-[5-tert-butyl-3-(2-dimethylamino-3,4-dioxocyclobut-1-enylamino)-2-methoxyphenyl]-3-[4-(6-morpholin-4-ylmethylpyridin-3-yl)naphthalen-1-yl]urea. Preferred title compds. inhibited TNF α production in THP cells with IC50<10 μ M.

ST heterocyclyl arylamide urea prepn antiinflammatory; tumor necrosis factor prodn inhibitor heterocyclyl arylurea prepn; cytokine mediated disease treatment heterocyclyl arylurea; dioxocyclobutenylaminomethoxyphenylmorpho
 lylmethylpyridinyl naphthalenylurea prepn drug

IT Inflammation

(Crohn's disease, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Intestine, disease

(Crohn's, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Nervous system, disease

(Guillain-Barre syndrome, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Respiratory distress syndrome

(adult, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Antiarteriosclerotics

(antiatherosclerotics; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Lung, disease

(chronic obstructive, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Dermatitis

(contact, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Inflammation

Intestine, disease

(enterocolitis, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Heart, disease

(failure, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Inflammation

Kidney, disease
 (glomerulonephritis, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Transplant and Transplantation
 (graft-vs.-host reaction, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Dialysis
 (hemodialysis, syndrome treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Heart, disease
 (infarction, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Reperfusion
 (injury, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Analgesics
 Anti-Alzheimer's agents
 Antiarthritics
 Antiasthmatics
 Antidiabetic agents
 Human
 (preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Injury
 (reperfusion, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Bone
 (resorption, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Tumor necrosis factors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (secretion inhibitors; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Brain, disease
 (stroke, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Shock (circulatory collapse)
 (toxic shock syndrome, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Polymorphonuclear leukocyte
 (transfusion syndrome treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Cytokines
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (treatment of cytokine-mediated disease; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Burn
 Lupus erythematosus
 Meningitis
 Multiple sclerosis
 Psoriasis
 Sepsis
 Skin, disease
 (treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT Inflammation
 Intestine, disease
 (ulcerative colitis, treatment; preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT 294850-71-8P 294851-09-5P 404009-23-0P
 404009-26-3P 404009-31-0P 404009-33-2P
 404009-35-4P 404009-37-6P 404009-39-8P
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 404010-20-4P 404010-22-6P 404010-24-8P
 404010-26-0P 404010-28-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT 98-09-9, Benzenesulfonyl chloride 110-91-8, Morpholine, reactions
 500-22-1, 3-Pyridinecarboxaldehyde 591-19-5 624-28-2 683-57-8
 930-68-7, 2-Cyclohexen-1-one 1072-72-6 1072-97-5 1445-73-4
 1899-24-7 1943-83-5 2298-07-9 3535-88-4 5222-73-1 5396-38-3,
 4-tert-Butylanisole 5414-19-7 29943-42-8 89364-31-8 168169-11-7
 294851-95-9 294853-07-9 404011-03-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT 6309-59-7P 21926-00-1P 71897-83-1P 77055-30-2P 79710-86-4P
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 294852-76-9P 294852-78-1P 294852-80-5P 294852-84-9P 294852-86-1P
 294852-90-7P 294852-92-9P 294852-94-1P 294852-96-3P 404010-31-7P
 404010-33-9P 404010-35-1P 404010-37-3P 404010-39-5P 404010-41-9P
 404010-48-6P 404010-62-4P 404010-66-8P 404010-72-6P 404010-75-9P
 404010-77-1P 404010-78-2P 404010-79-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

IT 294850-71-8P

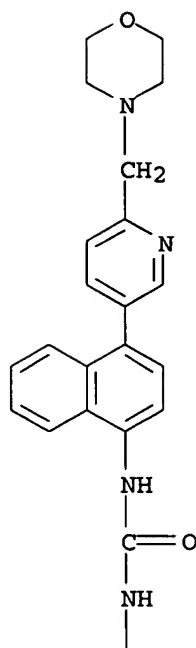
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of heterocyclyl arylamides and ureas as antiinflammatory agents)

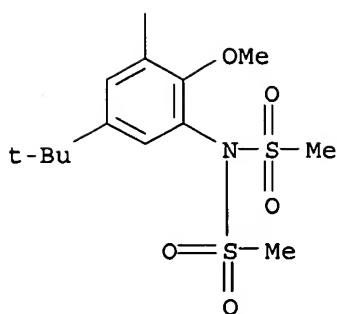
RN 294850-71-8 HCAPLUS

CN Methanesulfonamide, N-[5-(1,1-dimethylethyl)-2-methoxy-3-[[[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]amino]carbonyl]amino]phenyl]-N-(methylsulfonyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



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AN 2000:666713 HCAPLUS
DN 133:252426
ED Entered STN: 22 Sep 2000
TI Preparation of aromatic heterocyclic ureas as antiinflammatory agents
IN Betageri, Rajashehar; Breitfelder, Steffen; Cirillo, Pier
F.; Gilmore, Thomas A.; Hickey, Eugene R.; Kirrane, Thomas
M.; Moriak, Monica H.; Moss, Neil; Patel, Usha R.;
Proudfoot, John R.; Regan, John R.; Sharma, Rajiv; Sun,
Sanxing; Swinamer, Alan D.; Takahashi, Hidenori
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 282 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D231-38
ICS C07D213-38; C07D213-74; A61K031-44; A61K031-50; A61K031-415;

A61K031-505; C07D401-14; C07D405-12; C07D401-12; C07D213-76;
 C07D409-12; C07D493-08; C07D495-08; A61P029-00; C07D493-08;
 C07D307-00; C07D209-00; C07D495-08; C07D333-00

CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

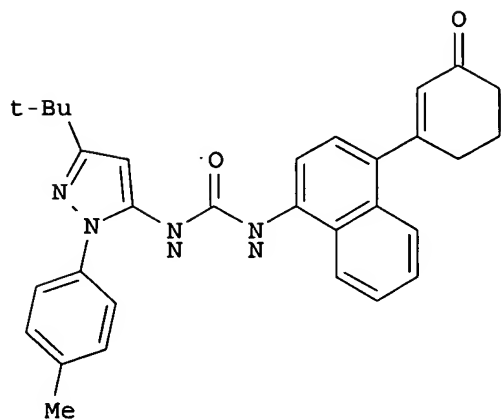
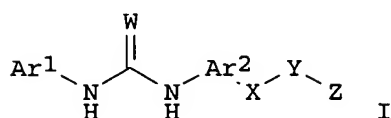
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CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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 OS MARPAT 133:252426
 GI



II

AB The title compds. (I) [wherein Ar1 = (un)substituted pyrrole, pyrrolidine, pyrazole, imidazole, oxazole, thiazole, furan, or thiophene; Ar2 = (un)substituted Ph, (tetrahydro)naphthyl, (tetrahydro)quinoline, (tetrahydro)isoquinoline, benzimidazole, benzofuran, indanyl, indenyl, or indole; W = O or S; X = (un)substituted cycloalkyl, cycloalkenyl, Ph, furan, thiophene, pyrrole, imidazolyl, pyridine, pyrimidine, (dihydro)pyridinone, (dihydro)maleimide, piperidine, piperazine, or pyrazine; Y = a bond or (un)substituted saturated or unsatd. alkyl optionally interrupted by O, NH, S(O), SO2, or S; Z = (un)substituted Ph, pyridine, pyrimidine, pyridazine, imidazole, (tetrahydro)furan, thiophene, (tetrahydro)pyran, 1,3-dioxolanone, 1,3-dioxanone, 1,4-dioxane,

(thio)morpholine (sulfoxide), piperidine, cyclohexanone, pentamethylene sulfoxide, etc.) were prepared for the treatment of diseases or pathol. conditions involving inflammation, such as chronic inflammatory diseases. Thus, coupling 2-cyclohexenone with 4-bromo-1-naphthylamine in the presence of Pd(PPh₃)₂Cl₂, DPPP, and NaHCO₃ in DMF, followed by conversion of the amine to an isocyanate using ClCOC₂ and immediate addition of 1-(4-methylphenyl)-3-tert-butyl-1H-pyrazol-5-amine, gave the urea II. In a cytokine production inhibition assay, preferred compds. of the invention showed IC₅₀ < 10 μ M against TNF- α in lipopolysaccharide stimulated THF cells.

ST arom heterocyclic urea prepn antiinflammatory agent; pyrazolyl arom urea prepn tumor necrosis factor inhibitor; urea arom heterocyclic prepn cytokine inhibitor

IT Anti-inflammatory agents

(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)

IT Tumor necrosis factors

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)

(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)

IT 294851-78-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)

IT 59-48-3, Oxindole 68-12-2, reactions 75-97-8 95-92-1, Diethyloxalate 109-77-3, Malononitrile 110-91-8, Morpholine, reactions 353-07-1, 2-Cyanoethylhydrazine 500-22-1, Pyridine-3-carboxaldehyde 585-34-2, 3-tert-Butylphenol 591-19-5, 3-Bromoaniline 624-28-2, 2,5-Dibromopyridine 626-35-7, Ethyl nitroacetate 628-22-8, 3-Cyano-1-propanol 930-68-7, 2-Cyclohexenone 1072-72-6, Tetrahydro-1,4-thiopyrone 1072-97-5, 2-Amino-5-bromopyridine 1445-73-4, 1-Methyl-4-piperidone 1461-22-9, Tributyltin chloride 1899-24-7, 5-Bromo-2-furaldehyde 2298-07-9, 4-Bromo-1-naphthylamine 3549-23-3, Methyl 4-tert-butylphenylacetate 4097-49-8, 4-tert-Butyl-2,6-dinitrophenol 5292-43-3, tert-Butyl bromoacetate 5414-19-7, Bis(2-bromoethyl) ether 6628-77-9, 5-Amino-2-methoxypyridine 7693-46-1, 4-Nitrophenylchloroformate 29943-42-8, Tetrahydro-4-pyranone 35944-64-0, 3-Iodo-4-methylphenylamine 59997-51-2, 4,4-Dimethyl-3-oxopentanenitrile 62559-08-4, 4-tert-Butyl-2-nitrotoluene 89364-31-8, Tetrahydro-3-furoic acid 155959-13-0, 2-tert-Butyl-6-chloro-5-methylpyridine-4-carboxylic acid methyl ester 168169-11-7 285984-25-0 285984-47-6 294853-00-2 294853-07-9 294853-09-1, 5-tert-Butyl-2-methoxyphenylacetic acid

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)

IT 294849-72-2P

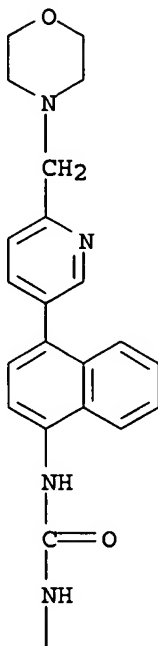
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aromatic heterocyclic urea antiinflammatory agents by conversion of arylamines to isocyanates followed by addition of heterocyclic amines)

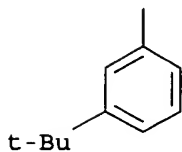
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CN Urea, N-[3-(1,1-dimethylethyl)phenyl]-N'-[4-[6-(4-morpholinylmethyl)-3-pyridinyl]-1-naphthalenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



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